## REMARKS/ARGUMENTS

Claims 1, 3-8 and 10-27 are pending in the application and presented for examination. Claims 1, 25 and 27 have been amended. The amendment to claims finds support for example, at page 3, lines 18-19. No new matter has been introduced with the foregoing amendment to the claims. Reconsideration of the application is respectfully requested.

In order to expedite prosecution of this application, Applicants have amended claims 1, 25 and 27 to recite that substantially no drug is contained in the outer layer of the inventive tablet.

## I. REJECTION UNDER 35 U.S.C §102(b)

The Examiner has rejected claims 1, 3, 4, 7, 8, 11, 12, 14-19, 24 and 27 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,922,352 ("Chen *et al.*"). In response, Applicants respectfully traverse the rejection.

Chen *et al.* teach a tablet having a delayed-release core and an outer extended-release coating that provides bioequivalent pharmacokinetic performance (i.e., *maintains* a sustained 24 hour drug plasma level) for a calcium channel blocker when compared with the commercially available Adalat CC tablet, which contains the calcium channel blocker nifedipine and has a rapid release core and a extended release external coat. (See, column 2, lines 45-52).

According to Chen *et al.*, the core of the controlled-release tablet contains a micronized crystalline calcium channel blocker. The micronized crystalline calcium channel blocker such as nifedipine is combined with an ***enteric coating agent*** which may contain a suitable plasticizer and a solid pharmaceutical acceptable filler or solid diluent. A preferred micronized nifedipine will have a surface area of 5 $m^2/g$ or higher. (See, column 2, lines 58-68).

Chen *et al.* relate to a tablet having a delayed release core, wherein the core has an enteric material. Thus, the tablet according to the teaching of Chen *et al.* is affected by a change in pH. For example, under the "Summary of the Invention," as well as claim 1, Chen *et al.* clearly disclose a core including "(i) particles of a calcium channel blocker compound ***coated with an enteric polymer*** that are dispersed onto a solid pharmaceutical filler." [Emphasis

added]. In order to achieve controlled-release or delayed-release of the calcium channel blocker in the colon, the enteric polymer "protects" the active ingredient in the low pH environment of the stomach.

> Under MPEP § 2131:
>
> [a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Unlike the teaching of Chen *et al.*, the current invention is drawn to a ***time-release tablet***, wherein the release of the active agent is unaffected by a change in pH. Applicants' invention is for a timed-release formulation, that is a tablet having at least ***two distinct layers*** each comprising a different formulation. The two distinct layers of the inventive formulation are:

1) a core tablet that has a drug and a freely erodible filler, wherein the core tablet erodes approximately 40% to approximately 90% in the digestive tract of the subject; and

2) an outer layer having a hydrogel-forming polymer substance, and a hydrophilic base, and substantially no drug.

Timed-release means, for example, that after a specific lag time, the drug from the pharmaceutical preparation is released. In the present invention, timed-release is achieved by the specific formulation of the core tablet and outer layer. The core-tablet layer of the of the multi-layered time-release formulation ***does not*** substantially contain a hydrogel polymer. Further, the outer layer substantially contains no drug. These features are not taught or suggested by Chen *et al.* As such, all the limitation of the claims are not found in Chen *et al.* and thus, the claims are not anticipated.

Further, Applicants respectfully traverse the Examiner's characterization of the claim as "a product-by-process" claim (see, paragraph 5 of the Office Action). As set forth in the M.P.E.P § 2173.05(p), a product-by-process claim is a product claim that defines the claimed product in terms of the process by which it is made. The instant claim recites:

> a) *a core tablet comprising a drug and a freely erodible filler, wherein said core tablet erodes approximately 40% to* approximately *90% in the digestive tract of said subject, wherein said core tablet does not substantially contain a hydrogel-forming polymer.*

The foregoing characterization is a feature of the claimed product. It is **not** how the product is made. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

## II. FIRST REJECTION UNDER 35 U.S.C §103(a)

The Examiner has rejected claims 5, 6, 10, 13, 21, 22, 23 and 25 under 35 U.S.C. § 103(a) as allegedly being obvious over Chen *et al.,* in view of EP 0 661 045 A1 ("Nakashima *et al.*"). In response, Applicants respectfully traverse the rejection.

As set forth in M.P.E.P. § 2143:

> [t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure.
>
> *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)

All three elements set forth above must be present in order to establish a prima facie case of obviousness. Applicants assert that a *prima facie* case of obviousness has not been established for the following reasons: 1) there is no suggestion or motivation to modify the references; 2) there is no reasonable expectation of success; and 3) the cited art references do not teach or suggest all the claim limitations.

**1. There is no Suggestion or Motivation to Modify the References**

Applicants state that there is simply no motivation or suggestion provided in the cited references to modify their teaching in the way the Office Action has contemplated. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The present invention relates to a timed-release compression-coated formulation. Timed-release means, for example, that after a specific lag time, the drug from the pharmaceutical preparation is released (See, Figure 1 of the specification). In the present invention, timed-release is achieved by the specific formulation of the core tablet and outer layer. The core tablet comprises the active ingredient and a freely erodible filler, and the outer layer comprises a hydrogel-forming polymer substance and hydrophilic base. Importantly, the core tablet is capable of approximately 40 to approximately 90% erosion. Surprisingly, Applicants have found that a percent erosion of the core tablet of approximately 40 to approximately 90% is necessary for an ideal timed-release pharmaceutical preparation having high bioavailability (See, page 4, lines 16-24 of the specification). Before the present invention, the requirement for 40 to approximately 90% erosion to obtain an ideal timed-release pharmaceutical preparation was ***unknown***.

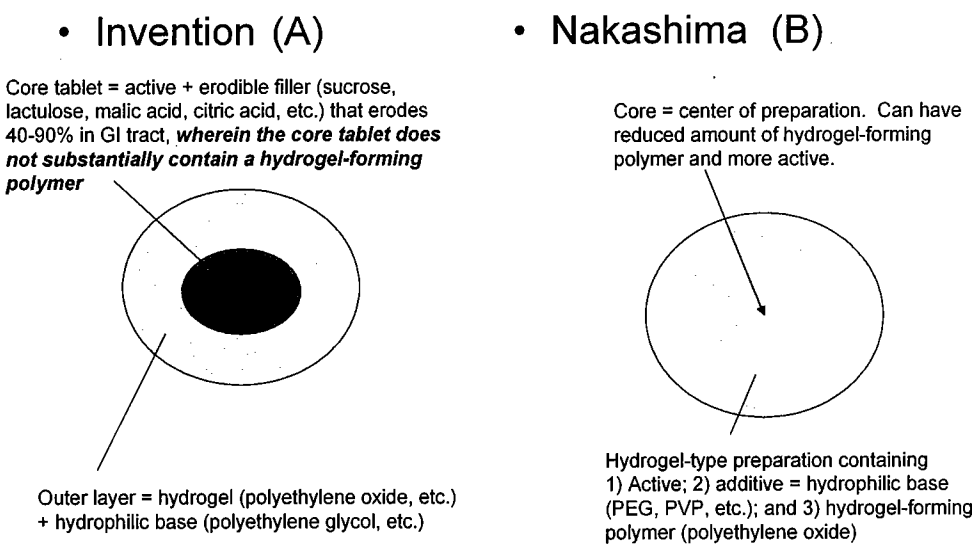
Chen *et al.* clearly disclose a core including "(i) particles of a calcium channel blocker compound ***coated with an enteric polymer*** that are dispersed onto a solid pharmaceutical filler." An enteric polymer is a feature of controlled-release. Chen *et al.* teach a tablet having a delayed-release core and an outer extended- release coating that provides bioequivalent pharmacokinetic performance (i.e., *maintains* a sustained 24 hour drug plasma level) for a calcium channel blocker. As such, there is simply no teaching or suggestion to modify the controlled-release features of Chen *et al.* to make it a timed-release formulation especially an

outer layer having a hydrogel-forming polymer substance, and a hydrophilic base, and substantially no drug as is currently taught and claimed.

Nakashima *et al.* do not supply the deficiencies of the primary reference. Nakashima *et al.* teach a sustained-release tablet in a single-layered formulation. Nakashima *et al.* teach a tablet that contains a *single-layer*, *i.e.*, a homogeneous formulation which comprises a i) a drug, ii) an additive providing for the penetration of water in to the core of the preparation, and iii) a hydrogel-forming polymer.

For the Examiner's convenience, a pictorial representation of the inventive tablet (A) and that of Nakashima (B), that clearly shows the differences in the two formulations is presented in Scheme 1 below. As set forth in the present claims, the core tablet in the inventive formulation ***does not*** substantially contain a hydrogel polymer. This is in clear contrast to the invention to Nakashima *et al.*, which is for a homogenous tablet comprising i) an active agent; ii) an additive, *e.g.*, a hydrophilic base; ***and iii) a hydrogel forming polymer***.

**Scheme 1**




As there is simply no teaching or suggestion to arrive at the claimed invention in view of the combination of references, the present invention is not rendered obvious. Accordingly, Applicants respectfully request that the rejection of the claims be withdrawn.

### 2. There is No Reasonable Expectation of Success

In addition, there is no reasonable expectation of success that the modification that the Office Action contemplates will succeed. "Both the suggestion and the expectation of success must be found in the prior art, not the Applicants' disclosure." *In re Dow Chem. Co.*, 5 USPQ2d 1529, 1532 (Fed. Cir. 1988).

Chen *et al.* clearly disclose a core including "(i) particles of a calcium channel blocker compound coated with an enteric polymer that are dispersed onto a solid pharmaceutical filler." An enteric polymer is a feature of controlled-release. Nakashima *et al.* teach a sustained-release tablet in a *single-layered* formulation. A skilled artisan would have no reasonable expectation of success in view of the combination of these references to arrive at the claimed invention of a timed-release formulation in a multi-layered composition comprising a core tablet and an outer layer, in which the core tablet does not substantially contain a hydrogel polymer. As such, Applicants respectfully request that the Examiner withdraw the rejection.

### 3. The Cited Art References Do Not Teach All Limitations of the Claims

The prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970). Applicants assert that the prior art references do not teach or suggest all the limitations of the claims and therefore, the obviousness rejection is untenable.

The combination of the references does not teach all the limitation of the claims. In fact, if a skilled person were to combine the teachings of Chen *et al.* and Nakashima *et al.*, the tablet would be a core of particles of an active ingredient coated with an enteric polymer that are dispersed onto a solid pharmaceutical filler as taught by Chen *et al.*, in a *single-layered* formulation as taught by Nakashima *et al.* These are not the features of the claimed invention. As such, Applicants respectfully request that the Examiner withdraw the rejection.

## III. SECOND REJECTION UNDER 35 U.S.C §103(a)

Claims 20 and 26 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Chen *et al.* in view of EP 0 709 386 A1 ("Taniguchi *et al.*"). In response, Applicants respectfully traverse the rejection.

Applicants respectfully assert that the dependent claims 20 and 26, which are dependent on independent claims 1 and 25, respectively, are not obvious over the combined disclosures of Chen *et al.* and Taniguchi *et al.* because the independent claims, *e.g.*, claims 1 and 25 are not obvious over the cited disclosures. In particular, Applicants respectfully assert that the cited references do not teach or suggest Applicants' claimed feature of a timed-release formulation in a multi-layered composition comprising a core tablet and an outer layer, in which the core tablet does not substantially contain a hydrogel polymer.

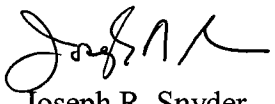
Chen *et al.* has been discussed and distinguished above. Taniguchi *et al.* teach benzazepeine compounds and pharmaceutical compositions thereof. Taniguchi *et al.* disclose a list of general pharmaceutical ingredients that can used to formulate a tablet composition comprising the benzazepeine compounds (*see*, page 27, lines 30-37). However, Applicants assert that there is no teaching or suggestion in Taniguchi *et al.* for a multi-layered timed-release tablet having a core tablet that does not substantially contain a hydrogel polymer. In view of the above, Applicants respectfully assert that the combined disclosures of Chen *et al.* and Taniguchi *et al.* do not teach or suggest the claimed invention. As such, Applicants respectfully request that the rejection be withdrawn.

## CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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